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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,060	06/10/2003	L. Gordon Letts	102258.157US1	8895

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WASHINGTON, DC 20006

EXAMINER	
ANDERSON, REBECCA L	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,060	LETTS ET AL.	
	Examiner	Art Unit	
	Rebecca L. Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 53-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 53* is/are rejected.

7)☒ Claim(s) *1, 2 and 53-55* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2 and 53-55 are currently pending in the instant application. Claims 1, 2 and 53-55 are objected and claims 1, 2 and 53 are rejected.

Election/Restrictions

In the response filed 30 June 2006, Applicants' representative argues that the restriction requirement is improper as the search and examination of the non-elected species would not place an additional burden on the Examiner. This argument is not found persuasive as the inventions are independent and distinct because there is no patentable co-action between the groups and a reference anticipating one member will not render another obvious. Each group is directed to art recognized divergent subject matter which require different searching strategies for each group. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner. Applicants' representative additionally argues that additional species upon an indication of allowability of the elected species pursuant to MPEP 803.02 should be examined. However, this is not found persuasive as prior art has been cited against the elected invention for search and examination. Additionally, it is noted that the restriction requirement is made under 35 U.S.C. 121. 35 U.S.C. 121 gives the Commissioner (Director) the authority to limit the examination of an application where two or more independent and distinct inventions are claimed to only one invention. The examiner has indicated that more than one independent and distinct invention is claimed in this application and has restricted (limited) claimed subject matter accordingly. Thus the

requirement to restrict the claims in this application is predicated on the fact that the claimed subject matter involves more than one independent and distinct invention. Nowhere do applicants argue to the contrary. Nowhere do applicants point out and give reasons why the claims do not involve independent or distinct subject matter. So, here we have claims, which involve more than one independent or distinct invention. Under 35 U.S.C. 121, the claims may be restricted and the examination limited to a restricted invention.

Therefore, **the elected invention for search and examination** is: the compounds and pharmaceutical compositions of the formula (I) wherein:

R5, R6, R7, R8, R9, R4 and **K** are as defined in claim 1;

X is an oxygen; and

T is an oxygen.

The requirement is still deemed proper and is therefore made FINAL.

Response to Amendments and Arguments

Applicants' amendment and arguments filed 30 June 2006 have been fully considered and placed in the application. Applicants' amendment deletes certain species from claim 54 and cancels withdrawn claims 3-52 and 56-81. Applicants' amendment does not overcome any objections or rejections. Applicant's arguments have been fully considered but they are not persuasive. In regards to the claim objections, applicant argues that the non-elected species should be rejoined. This is not persuasive for the same reasons as found in the above arguments and the objection to claims 1, 2 and 53-55 are maintained. In regards to the 35 USC 103 rejections of

claims 1 and 2 over Massie et al, Del Soldato et al. (WO 2001/012584), Del Soldato et al. (WO 95/30641), Benedini et al, or Eek et al., Applicants' representative argues that all of the references are non-analogous art as the references do not disclose or suggest nitrate esters of the highly selective cyclooxgenase-2 selective inhibitor of the present invention, known as COX-189 or lumiracoxib and cannot properly form the basis of an obviousness rejection for the nitrate esters of the selective cyclooxygenase-2-inhibitor of the present invention. This argument is not persuasive as the references provided are analogous art. Specifically, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant is concerned, in order to be relied upon as a basis for rejection of the claimed invention. See In re Oetiker, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Massie et al, Del Soldato et al. (WO 2001/012584), Del Soldato et al. (WO 95/30641), Benedini et al, and Eek et al. are considered analogous art as the references disclose anti-inflammatory compounds which generically overlap with applicants' instantly claimed compounds differing by a hydrogen versus a methyl. The prior art references provide nitrate esters of anti-inflammatory compounds which is considered analogous art.

Applicant also argues that none of the references disclose the compounds of the present invention and the compounds claimed are structurally different from the compounds or the prior art references and have different pharmacological properties from the prior art compounds. Applicants' argument has been considered but is not persuasive. Specifically, the prior art references disclose compounds which generically

overlap with applicants' instantly claimed compounds, the difference being a hydrogen versus a methyl. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. Furthermore, the halogens found on the generic disclosure of the compounds are sufficiently limited and well delineated.

In support of the difference in the pharmacological properties for the non-steroidal anti-inflammatory compound, diclofenac, disclosed by Massie, and the selective cyclooxygenase-2 inhibitor of formula (I), lumiracoxib, of the present invention, applicant provides a table wherein the inhibitory potencies for the TxB2, PGE2 and COX-2 selectivity are 0.097um, 0.013um and 7 respectively and wherein the inhibitory potencies for the TxB2, PGE2 and COX-2 selectivity for lumiracoxib are 67um, 0.13um and 515 respectively. In regards to the difference in pharmacological properties, it is noted that a difference in pharmacological properties does not indicate unobvious results over the prior art references. This data merely provides a showing that both compounds are useful as anti-inflammatory compounds. Furthermore, Attorney's arguments of unexpected results cannot take the place of evidence in the record. There is no evidence of record to show and explain how these different properties provide unobvious results. Additionally, the pharmacological properties of lumiracoxib provide motivation and direction to modify the prior art compounds as the compound has anti-inflammatory activity.

Applicant also argues that there is no motivation for one skilled in the art to make the claimed nitrosated selective cyclooxygenase-2-inhibitor compounds based on the teachings of the prior art references. This argument is not found persuasive as it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the any of the prior art references as the references disclose compounds useful, for example, as anti-inflammatory and analgesic agents, which generically overlap with applicants' instantly claimed invention and differ from applicants' elected invention only by having a hydrogen versus a methyl or ethyl. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as anti-inflammatory agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

As applicants' arguments are not found persuasive, the 35 USC 103 rejections of the claims are maintained.

Maintained Claim Objections

Claims 1, 2 and 53-55 are objected to as containing non-elected subject matter. Claims 1, 2 and 53-55 presented drawn solely to the elected invention identified supra as: the elected invention for search and examination, would overcome this objection.

Claims 54 and 55 are also objected to as being dependent upon a rejected base claim, but would be appear allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and presented drawn solely to the elected invention as identified supra.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

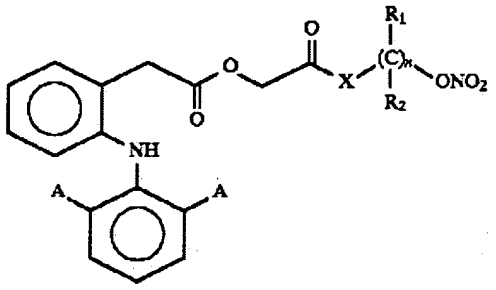
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,844,696 (SERRA).

Determining the scope and contents of the prior art

SERRA discloses the compounds of the formula (I) on column 1:



(I)

where:

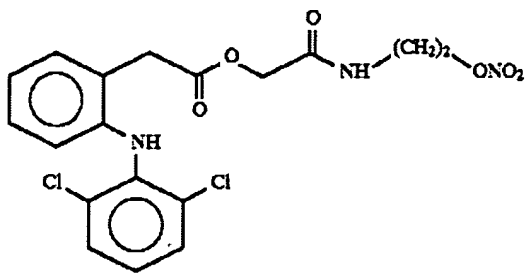
A is fluorine, chlorine or bromine;

X means oxygen, NH or NR where R means a linear or branched alkyl chain of 1 to 6 carbon atoms;

R_1 and R_2 mean, independently, hydrogen or a linear or branched alkyl chain of 1 to 6 carbon atoms; and

and n is a number between 1 to 10.

These compounds are useful as anti-inflammatory and analgesic agents (see column 1). Column 2 further discloses the compound of the formula III:



(III)

. While compounds wherein one A is fluorine is not specifically named, as seen in formula III wherein both A's are disclosed as Cl, and it is necessary to select portions of teachings within the reference and combine them, the compounds are still considered obvious because the substituents are sufficiently limited and well delineated, i.e. each A is either fluorine, chlorine or bromine. One of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula wherein one of A is fluorine and one is chlorine.

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

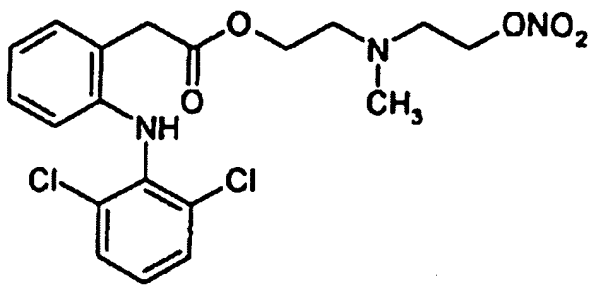
However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the prior art of SERRA. SERRA discloses the compounds of formula I and III which are useful as anti-inflammatory and analgesic agents, which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl

for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as anti-inflammatory agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Soldato (WO 2001012584).

Determining the scope and contents of the prior art

Del Soldato discloses compounds of the formula A-B-N(O)s (page 6) which are useful for, such as, anti-inflammatory agents (page 2). Specific compounds of formula A-B-N(O)s are disclosed, such as, the formula of example 14, page 49:



Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the prior art of Del Soldato. Del Soldato discloses the compounds, such as example 14, which are useful as anti-inflammatory agents which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists

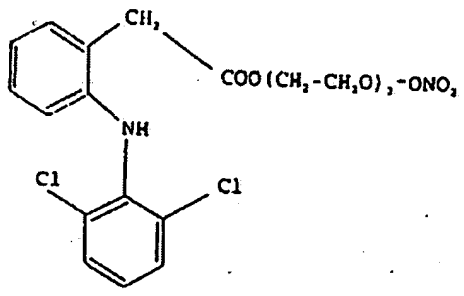
knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as anti-inflammatory agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Soldato et al. (WO 95/30641).

Determining the scope and contents of the prior art

Del Soldato et al. discloses the compounds of formula A-X1-NO2 (page 6) which have anti-inflammatory and analgesic activity (page 1) such as the compound of the formula of Example 1b (page 43):

2-{N-[2,6-(dichloro)phenyl]amino}phenylacetate of 2-[2-(nitroxy)ethoxy]ethyl



Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

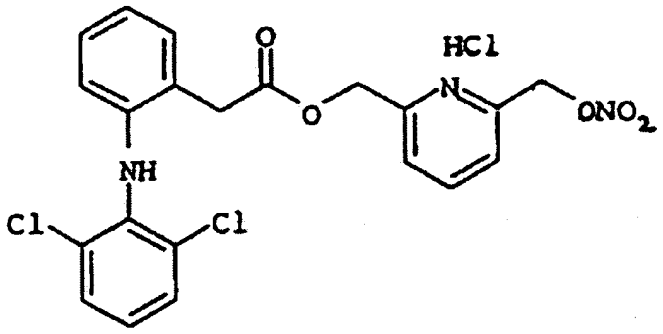
However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the prior art of Del Soldato et al. Del Soldato et al. discloses the compounds, such as the formula of example Ib, which are useful as anti-inflammatory agents which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as anti-inflammatory agents.

Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benedini et al. (WO 2000051988).

Determining the scope and contents of the prior art

Benedini et al. discloses the compounds of formula A-X1-N(O)z (page 4) which have anti-inflammatory and analgesic activity (page 1) such as the compound of the formula of Example 13 (page 46):



Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

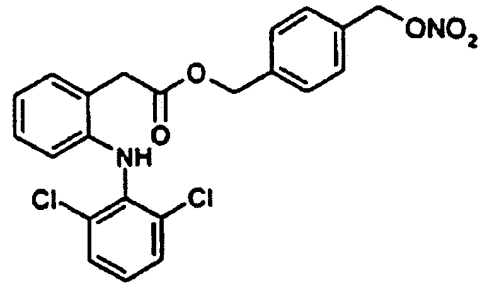
However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the prior art of Benedini et al.

Benedini et al. discloses the compounds, such as example 13, which are useful as anti-inflammatory agents which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as anti-inflammatory agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eek et al. (WO 2000072838).

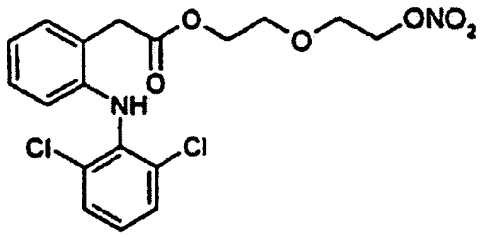
Determining the scope and contents of the prior art

Eek et al. discloses the compounds of the formula (I), M-C(=O)-O-X-ONO2 on page 3 which are useful as antibacterial agents (page 1). Specific compounds of formula (I) are found on pages 6 (formula Ii) and 7 (formula (IL):



(Ii)

and



(IL)

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the prior art of Eek et al. Eek et al. discloses the compounds of formula (I) such as (Ii) and (IL) which are useful as antibacterial agents which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137

U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as antibacterial agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KAMAL A. SAEED, PH.D.
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9/14/06

for Joseph K. McKane
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Technology Center 1600